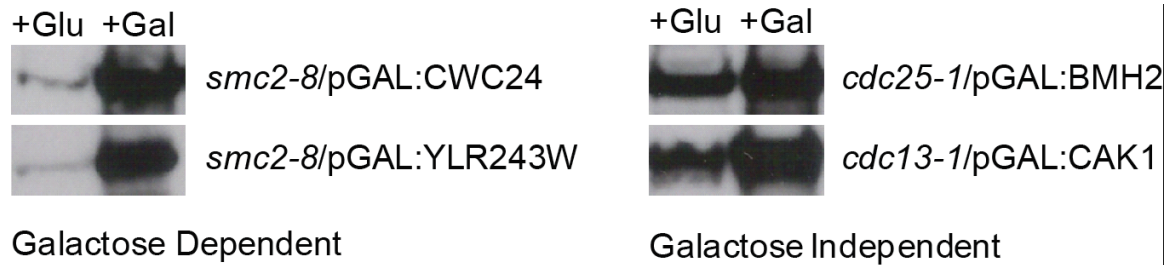


Supplementary Figure S1

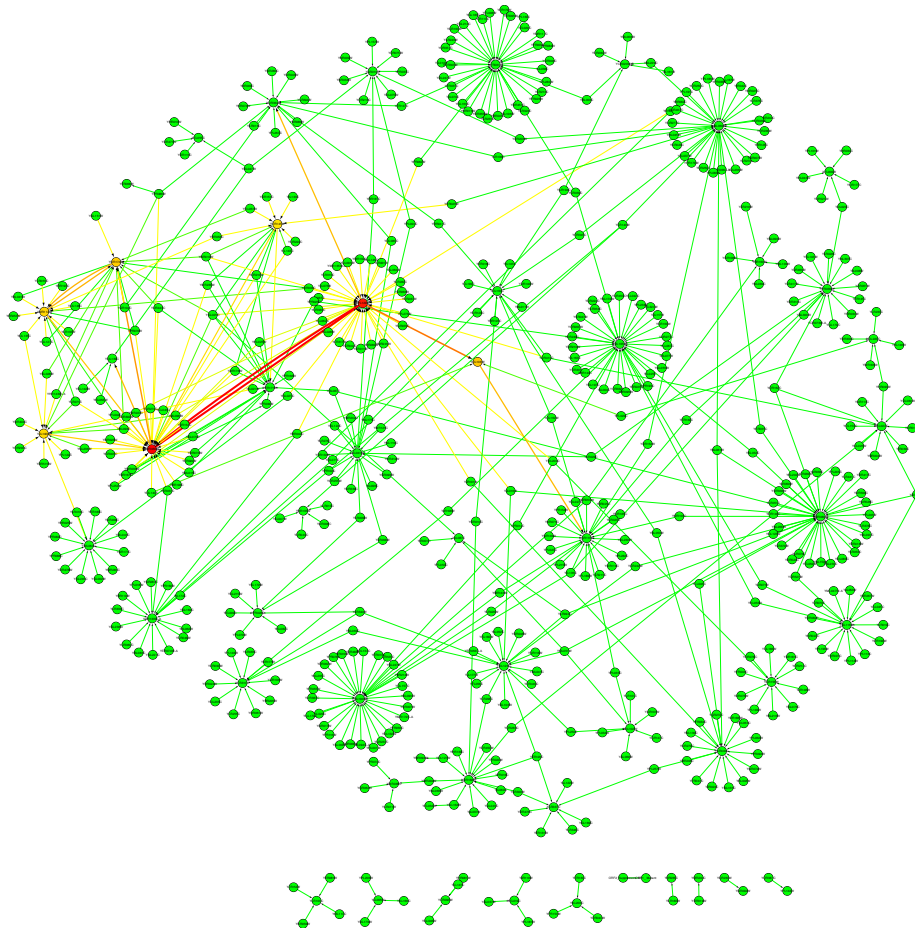
Example MORF protein expression in presence or absence of galactose.

Galactose dependency of dosage suppression determined by Western blotting: *ts* mutant strains harboring CWC24, YLR243W, BMH2 and CAK1 MORFs grown in presence of glucose and galactose separately and proteins extracted, equal amount of proteins blotted to PVDF membrane and probed with anti-HA antibody. CWC24 and YLR243W are galactose dependent; BMH2 and CAK1 are galactose independent.

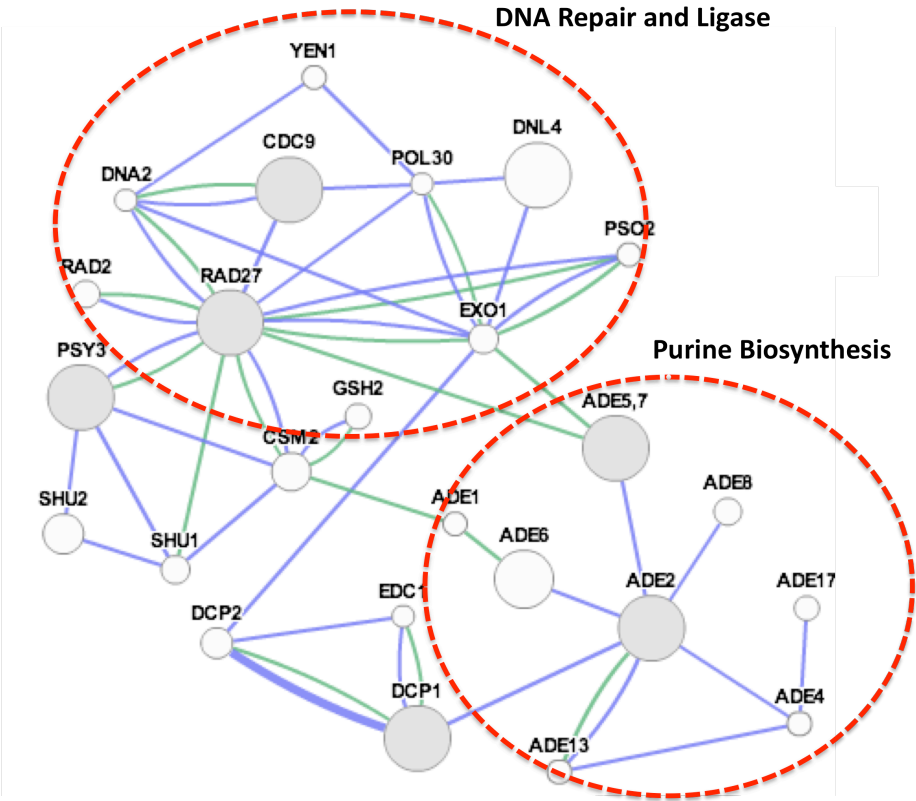


Supplementary Figure S2

Dosage suppressor network of 53 *ts* lethal mutations. 660 interactions were discovered through the general screen and several focused screens. Nodes are either essential gene mutations or their suppressors, and the directed edges (color and thickness weighted by edge-betweenness centrality) are dosage suppressor interactions. Many suppressors are likely specific to the experimental conditions adopted here, and at least a subset may be allele specific. Alternate experimental methods may reveal additional suppressors. See **Cytoscape File:** <http://tinyurl.com/l794oq9>.

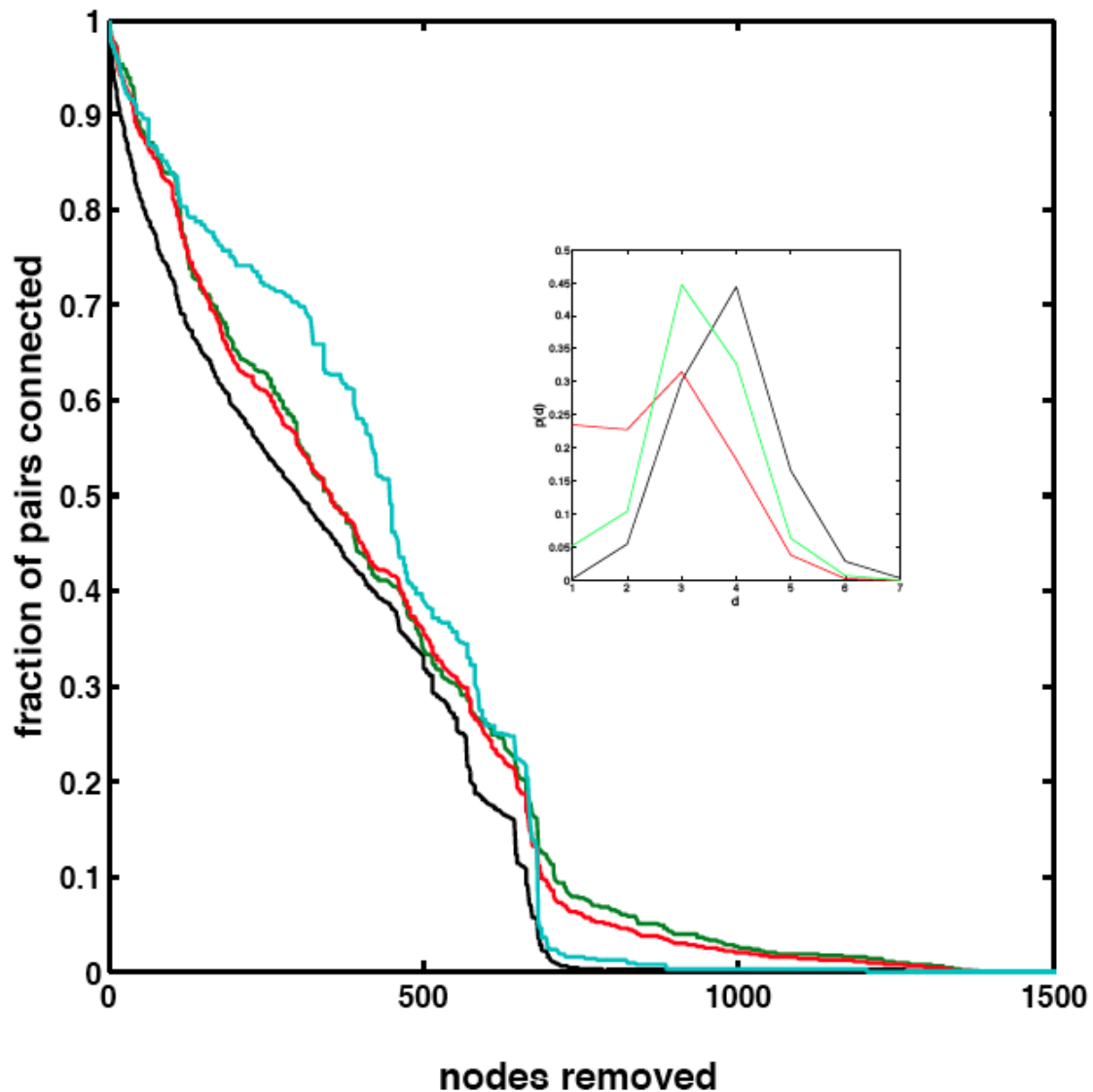


Supplementary Fig S3



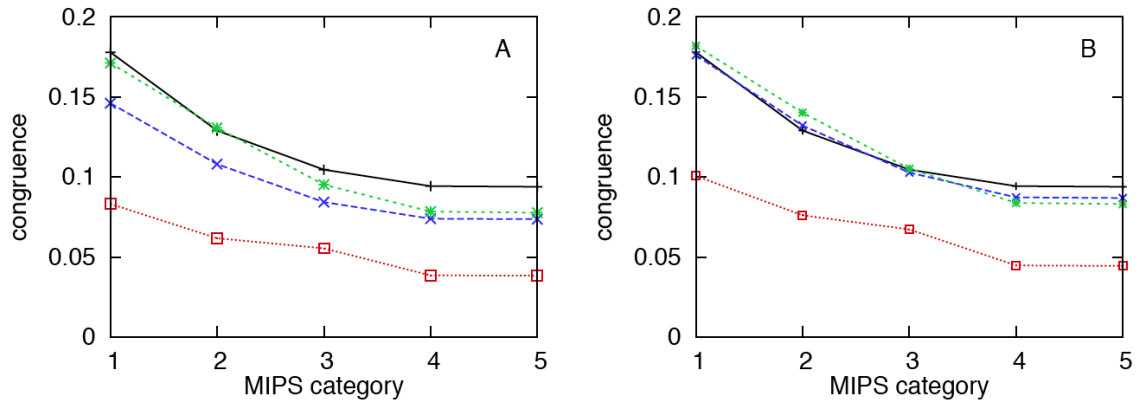
Supplementary Fig. S4: Fraction of node pairs connected within the PPI network upon removal of genes with descending BC (betweenness centrality).

Black: fraction of all gene pairs that remain connected (the control). Cyan: Fraction of genes in the suppressor network described here that remain connected. Red: fraction of pairs from the suppressor network in the BioGRID database that remain connected. Green: fraction of pairs in the network described in Magtanong *et al.* (2011) that remain connected. Inset: distribution of pairwise distances (in terms of edges of the PPI network) in the PPI network (black, control), the BioGRID suppressor network (red), and the suppressor network described here (green).



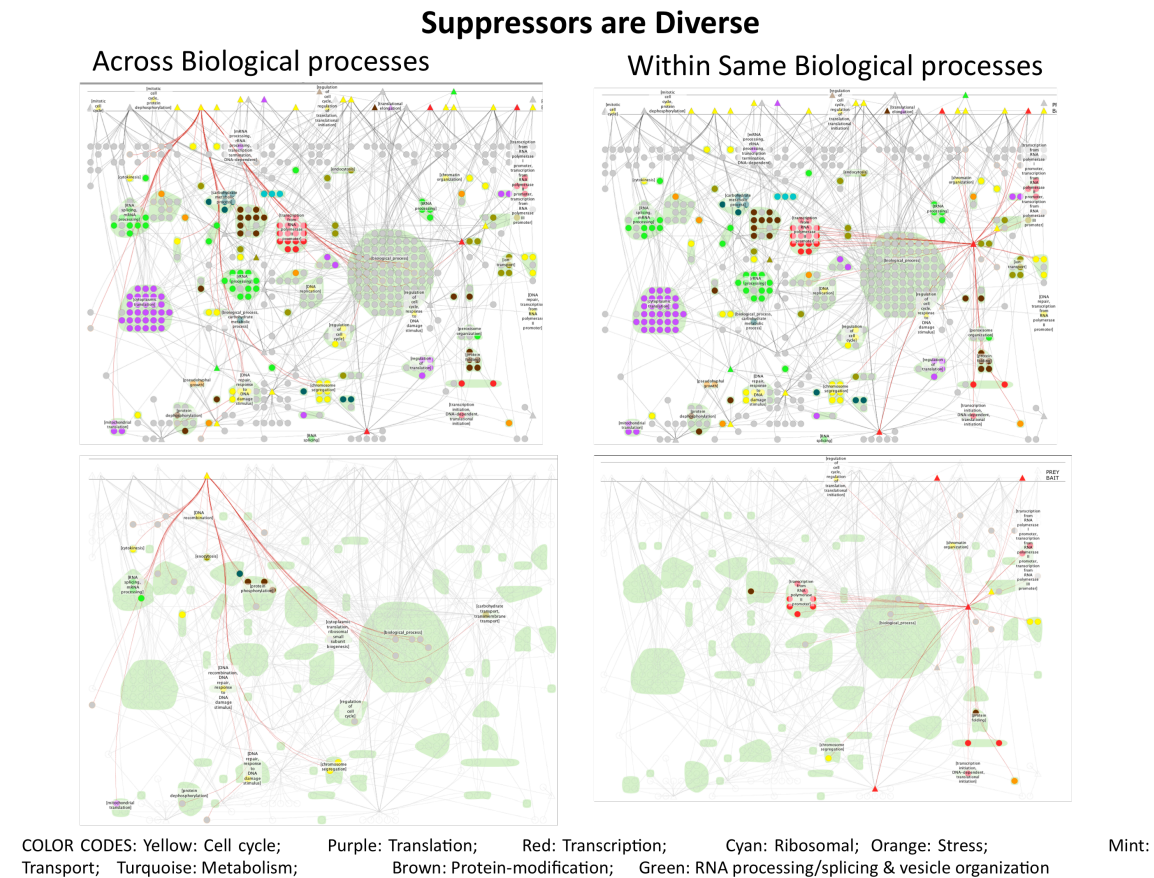
Supplementary Fig. S5A: Functional congruence between ts-mutants and their suppressors. Red (dotted): congruence between mutants and their suppressors for the pairs described in this work, as a function of the MIPS category. Congruence decreases with increasing category because function becomes more and more specialized. Blue (long-dashed): congruence from pairs reported in the BioGRID database. Green (short-dashed): pairs reported in Magtanong *et al.* (2011). Black: congruence between proteins that share an edge in the curated PPI for comparison.

Supplementary Fig. S5B: Functional congruence among co-suppressors of the same ts-mutant. Red (dotted): congruence between suppressors of a mutant for the pairs described in this work, as a function of the MIPS category. Blue (long-dashed): congruence from pairs reported in the BioGRID database. Green (short-dashed): pairs reported in Magtanong *et al.*, (2011). Black: congruence between proteins that share an edge in the curated PPI (same as in Fig. S4A).



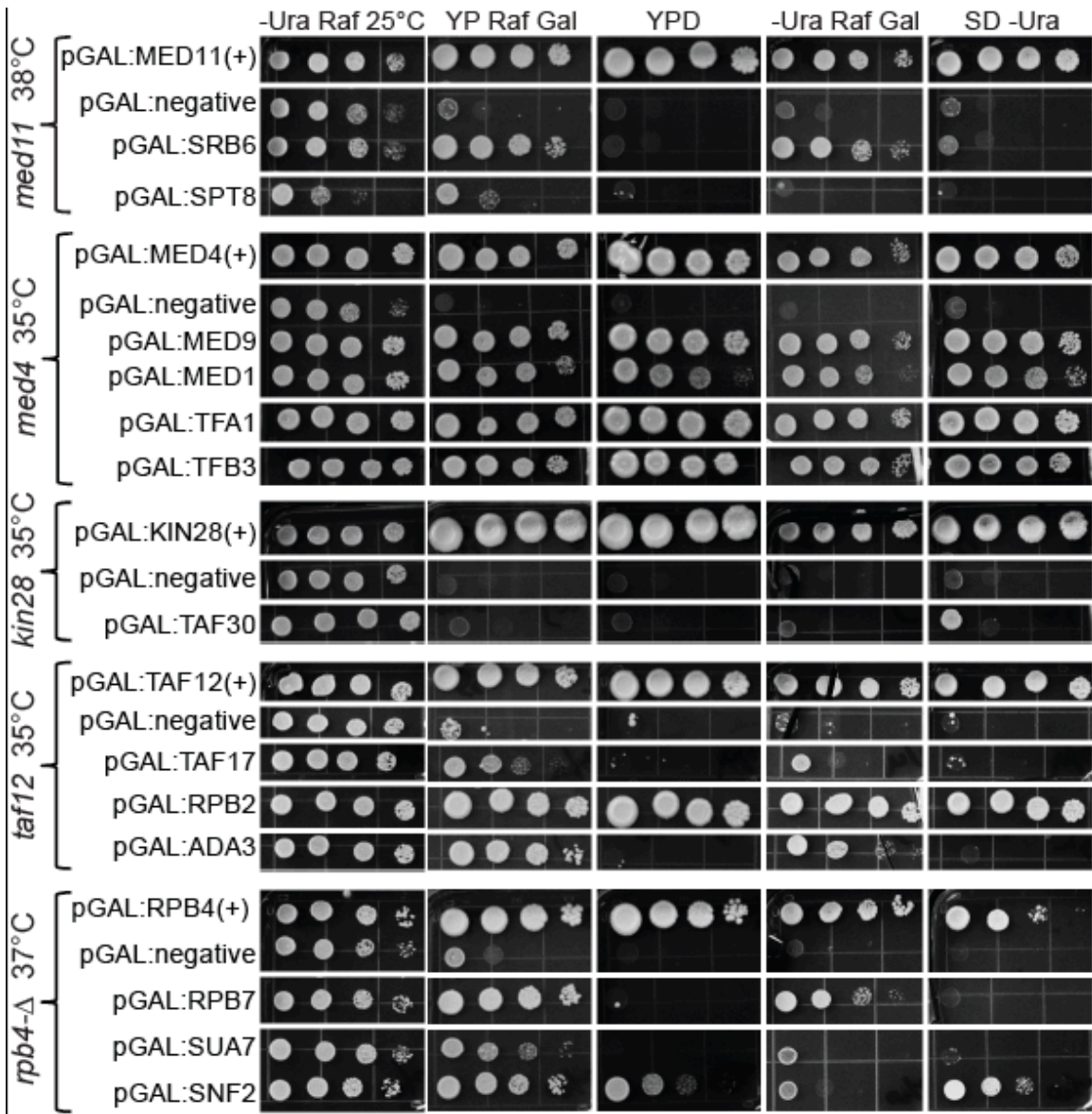
Supplementary Figure S6

Dosage suppressors are functionally diverse. Examples from the dosage suppressor network illustrating the functional diversity between co-suppressors of the same mutant. The suppressed mutations and their suppressors are organized by their GO ontologies in two dimensions. While co-suppressors of the same mutation are usually related by GO cellular processes (they are closely located along the horizontal axes), there are also many cases where the co-suppressors belong in disparate cellular processes (distributed along the vertical axes). Nodes are colored by Gene Ontology and grouped into green patches representing common biological processes. Triangles depict mutants and circles represent suppressors. Selected edges are colored in red to illustrate functional homogeneity (co-suppressors are on similar planes) or heterogeneity (co-suppressors are in different planes) among co-suppressors. GO color codes: Yellow: Cell cycle; Purple: Translation; Red: Transcription; Cyan: Ribosomal; Orange: Stress; Mint: Transport; Turquoise: Metabolism; Brown: Protein-modification; Green: RNA processing/splicing & vesicle organization. The nodes classified by molecular function are distributed along the x-axis and by biological process along the y-axis. A few selected edges are colored in red to illustrate functional homogeneity (co-suppressors are on similar planes) or heterogeneity (co-suppressors are in different planes) of co-suppressors.



Supplementary Figure S7:

Examples of dosage suppressors of RNA Pol II mutants.



Supplementary Figure S8

Quantitative RT-PCR validation of two microarray gene expression data.

